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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/742,148	BUELOW, ROLAND	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,16 and 17* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/24/03 is acknowledged.

Claims 13-17 are pending.

Claims 13-17 read on a compound comprising an oligopeptide of SEQ ID NO:3 and are under consideration in the instant application.

2. If applicant desires priority under 35 U.S.C. 119 (e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

In view of the amendment, filed 11/24/03, the following rejections remain

2. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 13 and 16 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 13 is indefinite and ambiguous in the recitation of: " a compound comprising an oligopeptide of at least 6 amino acids,.... including amino acids 84 to 86". The claim as written encompass an oligopeptide of 6 amino acid. It is unclear how an oligopeptide of only 6 amino acid can have amino acids 84 to 86 ? If Applicant means that oligopeptide includes the triad

YYW (SEQ ID NO;1) sequence corresponding to positions 84-to 86 of the HLA-B α1 domain sequence, then he should clearly stated that for clarity and consistence with the disclosure of the specification.

B. Claim 16 is indefinite and ambiguous in the recitation of " ... according of Claim 15 of at least 10 amino acids ..." The claim as written encompass an oligopeptide of 10 amino acid, however the base claim 15 recited a compound consisting of 14 amino acids.

Applicant's argument, filed 11/24/03 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) claim 13 has been rephrased to expressly state the compound implicit in the prior filed claims ; (ii) claim 16 has been amended to expressly state subject matter in the prior filed claim.

Contrary to Applicant's assertion: (i) the amended claim 13 still recited "a compound comprising an oligopeptide of at least 6 amino acids,.... including amino acids 84 to 86 ". The claim as written encompass an oligopeptide of 6 amino acid. It is unclear how an oligopeptide of only 6 amino acid can have amino acids 84 to 86 ? (ii) the amended claim 16 still recited " ... according of Claim 15 of at least 10 amino acids ..." The claim as written encompass an oligopeptide of 10 amino acid, however the base claim 15 recited a compound consisting of 14 amino acids.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 13, 14, 16 and 17 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound consisting of specific oligopeptide SEQ ID NOs 3-56 does not reasonably provide enablement for: (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 5/20/03.

Applicant's arguments, filed 11/24/03 have been fully considered, but have not been found convincing.

Applicant asserts that Claims 13 and 14 recites oligopetides in which amino acid recidue are well known and well defined and that methods for synthesizing these peptides either chemically or recombinantly are well known in the art and they can be readily made and used without undue experimentation given the knowledge of peptide synthesis and guidance provided in the specification; the working examples in the Specification disclosed an oligopeptides comprising the recited structure.

Contrary to Applicant's assertion the issue raised by the Examiner was not about methods of synthesizing peptides, but rather that Applicant only discloses an oligopeptides consisting of SEQ ID NOS: 3-56 that can modulate lymphocyte activity in the instant specification (see pages 15-18 in particular). Applicant has not taught how to make and use i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 that can modulate lymphocyte activity. The structural and functional characteristics of said oligopeptides are not defined in the specification and in the claims. The specification fails to provide sufficient guidance as to which core structure of SEQ ID NOs: 3-56 is essential for maintain their activity and which changes can be made in the structure of SEQ ID NOs 3-56 and still maintained the same function. Moreover, Applicant himself acknowledge that only a specific sequences including amino acids at specific position are permitted to performed the claimed modulation of lymphocyte activity (see page 10, lines 10-20 in particular). Applicant also stated that among oligopeptide comprising the recited structures only several maintained their activity and protein E, for example, has no activity at all (see page 22, lines 5-30 in paricular).

"Comprising" is considered open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 includes an unlimited number of amino acid sequences "comprising" an unlimited number of polypeptides. The disclosure of SEQ ID NOS: 3-56 cannot support the entire genus of *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW,

corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 as part of their sequence that maintained the same function.

Also an issue is that Applicant has not taught how to make and use a compound comprising an oligopeptide of 6 amino acids wherein amino acids 84 to 86 are YYW, as claimed in claim 13. The claim as written encompass an oligopeptide of 6 amino acid. It is unclear how one skill in the art can make an oligopeptide of only 6 amino acid that will have triad YYW at position 84 to 86 as part of their sequence?

Applicant is relying upon certain biological activities and the disclosure of a limited number of species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 encompassed by the claimed invention other than "a compound consisting of specific oligopeptide SEQ ID NOs 3-56" would be expected to have greater differences in their activities.

Since the amino acid sequence of a polypeptide determined its structural and functional properties, predictability of which fragments will retain functionality requires knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence contribute to its structure, and therefore, function. The problem of predicting which fragments or derivatives of a protein will retain functionality and which will not is complex and well outside the realm of routine experimentation. Because of the lack of sufficient guidance and predictability in determining which structures would lead to functional proteins or peptides with the desired properties and that the relationship between the sequence of a peptide and it's tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al, in The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encompassed by the claimed invention. Without sufficient guidance, the changes which can be made in the structure of "*any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids

comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 " and still specifically modulate lymphocyte activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed (i *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

6 . Claims 13, 14, 16 and 17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 5/20/03.

Applicant is in possession of : a compound consisting of specific oligopeptide SEQ ID NOs 3-56.

Applicant is not in possession of : (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17.

Applicant's arguments, filed 11/24/03 have been fully considered, but have not been found convincing.

Applicant asserts that HLA-B α1 domain was understood and comprehended in the art by its structure, chemical name and sequence such that attributes common to the domain were well

known in the art. The disclosure provides specific structural description of HLA-B α1 domain and associated bioactivity of the claimed peptides.

Contrary to Applicant's assertion, the specification fails to define *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 that can modulate lymphocyte activity .

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a protein by functional language in the absence of a structure is not considered sufficient to show possession of the claimed invention. See Fiers, 984 F.2d at 1169-71, 25 USPQ2D at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many species may achieve that result. The definition requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 /f.2d 1516, 1521, 22 USPQ 369, 372-73 (Fed. Cir. 1984) affirming the rejection because the specification does "little more than outline[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of (e.g. structural feature), is not a description of that material.

A description of a genus of protein sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in

possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. Claim 15 is objected to in being dependent upon rejected base claim 14, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. No claim is allowed

9. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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